

Remarks:

Claims 1-7, 9, 10, and 13 are currently pending in this application. Claim 9 has been withdrawn as being directed to a non-elected invention. Claims 3-5 have been canceled and claim 1 has been amended in this response.

The Examiner has acknowledged the effective filing date of the instant application and its foreign priority of February 4, 2004 and April 4, 2003 respectively. The Examiner has indicated the non-compliance of the IDS filed on September 21, 2005. Applicants will be submitting a revised copy of the IDS which complies with 37 CFR 1.98(a)(2) shortly.

35 U.S.C. §112

The Examiner has rejected claims 1-7, 10, and 13 under 35 U.S.C. §112 second paragraph as being incomplete for omitting essential structural cooperative relationships of elements. In the Examiner's view, the claimed combination "necessarily indicates that the drugs will be administered at the same time" which contradicts claim 1 which indicates that the anti-epileptics are for "simultaneous, separate or sequential use". Applicants have amended claim 1 to delete the intended usage.

35 U.S.C. §103(a)

The Examiner has rejected claims 1-7 as being obvious under 35 U.S.C. §103(a) over *Czuczwar* in view of *Deckers* and in further view of *Suter*. The Examiner asserts that *Czuczwar* teaches a combination of carbamazepine and LY300164, a dual AMPA/kainite receptor antagonist, for treating epilepsy. The Examiner acknowledges that *Czuczwar* does not teach AMP397. The Examiner next alleges that *Suter* teaches AMP397 and that AMP397 is a selective AMPA receptor antagonist and an anticonvulsant. The Examiner next asserts that *Deckers* teaches sequential monotherapy and polytherapy are good options for treatment of epilepsy and that it is advantageous to choose drugs with different mechanisms of action for such polytherapy. According to the Examiner, it would have been obvious to combine *Czuczwar*, *Suter*, and *Deckers* to create an anti-epileptic drug combination comprising carbamazepine and AMP397.

The Examiner further asserts that claims 1-7 and 10 are obvious under 35 U.S.C. §103(a) over *Levy* (U.S. Patent no. 5,095,033), in view of *Deckers*, and *Suter*. The Examiner asserts that *Levy* teaches a pharmaceutical composition comprising stiripentol and carbamazepine for the treatment of epilepsy. The Examiner admits that *Levy* fails to teach AMP397. The Examiner next asserts that *Deckers* teaches that it is advantageous to choose a drug with a different mechanism of action than the first for adding a second anti-epileptic to a treatment regimen. The Examiner further asserts that *Suter* teaches AMP397 is a selective AMPA receptor antagonist and an anticonvulsant. According to the Examiner, it would have been obvious to

combine *Levy*, *Suter*, and *Deckers* to create an anti-epileptic drug combination comprising carbamazepine and AMP397 by substituting the stirpental of *Levy* with the AMP 397 of *Suter*.

Lastly, the Examiner asserts that claim 13 is obvious under 35 U.S.C. §103(a) over *Czuczwar* in view of *Deckers* and *Suter* and in further view of *Weaver* (U.S. Patent No. 6,306,909). The Examiner again asserts that the combination of *Czuczwar*, *Deckers* and *Suter* teach the combination of carbamazepine and AMP397 and that *Weaver* teaches kits comprising anti-epileptic drugs.

Applicants first dispute that the Examiner has established a *prima facie* case of obviousness. The Patent Office has the burden of presenting factual evidence that would indicate that the claimed combinations are *prima facie* obvious. (*In re Lunsford*, 148 U.S.P.Q. 721 (C.C.P.A. 1966)). Such a *prima facie* case of obviousness requires that there be some teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce the claimed invention. (*In re Kahn*, 441 F.3d 977, 986; 78 U.S.P.Q.2d 1329, 1335 (Fed. Cir. 2006)). Additionally, there must be a reasonable expectation of success. (M.P.E.P. §2143). The Supreme Court has further clarified that the motivation to combine references need not be found explicitly, but may instead be implicit, in the prior art. (*KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398; 127 S.Ct. 1727, 1741 (2007)). In the absence of such a showing, such a rejection is based on impermissible hindsight. (*In re Fritch*, 972 F.2d 1260, 1266; 23 U.S.P.Q.2d 1780, 1784 (Fed. Cir. 1992) (“it is impermissible for an examiner, in proffering a 35 U.S.C. §103 rejection, to use the claimed invention as an instruction manual or “template” to piece together the teachings of the prior art to render the claimed invention obvious.”)).

Applicant respectfully submits that the Examiner, in combining the *Czuczwar*, *Suter*, and *Deckers* reference as well as the *Levy*, *Suter*, and *Deckers* references, has engaged in reconstructive hindsight. The Examiner essentially suggests that one of skill in the art would have been motivated to remove the LY300164 from *Czuczwar* and/or the Stiripentol from *Levy* and replace said compounds with the AMP397 of *Suter* because *Deckers* teaches that addition a second anti-epileptic to a treatment regime can be beneficial. However, both *Czuczwar* and *Levy* already teach a combination of two anti-epileptic drugs having different mechanisms of action. Thus there would be no motivation to select a different anti-epileptic drug and substitute it for either the LY300164 of *Czuczwar* or the Stiripentol of *Levy*. Likewise, there is no teaching or suggestion in *Suter* which would motivate one of skill in the art to combine AMP397 with any other anti-epileptic drug and certainly no teaching or suggestion that it should be combined with carbamazepine. The mere disclosure of *Deckers* that polytherapy could be used for treating epilepsy would not teach or motivate one of skill in the art to combine the particular combination of anti-epileptic drugs claimed by Applicant in the instant application. Indeed, *Deckers* does not even disclose AMP397.

Even assuming, *arguendo*, that a *prima facie* case of obviousness were established, the claimed invention is not obvious in view of its unexpectedly superior results. As demonstrated in ¶¶54-55 and Table 1 of the instant application, the claimed combination exhibits a more than additive anticonvulsant effect over what would be expected by combining mono-therapies. Applicant submits that in light of this evidence, claims 1-2, 6-7 and 10 of instantly claimed invention are not obvious over the cited references. As the combination of *Czuczwar*, *Deckers* and *Suter* do not render obvious a combination of carbamazepine and AMP397, Applicant respectfully submits that the addition of *Weaver* does not render claim 13, directed to a kit comprising the anti-epileptics of claim 1, obvious. All pending rejections having been traversed Applicant requests allowance of the currently pending claims.

Respectfully submitted,



Daniel J. Woods
Daniel J. Woods
Attorney for Applicants
Reg. No. 59,864

Novartis Pharmaceuticals Corp.
Patents Pharma
One Health Plaza, Building 104
East Hanover, NJ 07936-1080
(862) 778-9587

Date: *2/11/09*